The Pharmacist Activist

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Editorial

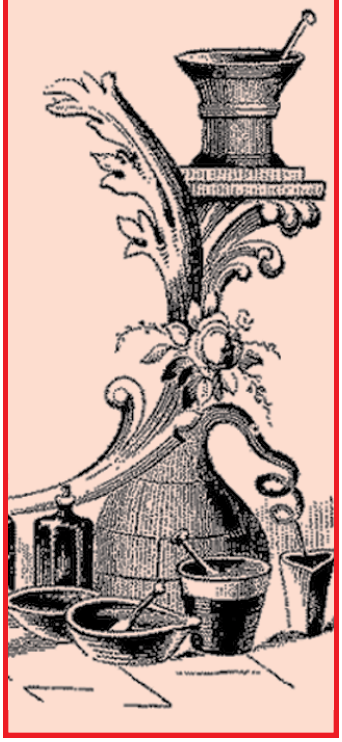
DRUG SHORTAGES – Pharmaceutical Companies Have Caused This Problem and it is Their Responsibility to Resolve it!

There have been numerous concerns voiced about the high cost of prescription medications to which the pharmaceutical companies have responded that this level of revenue is necessary to support their extensive research programs that will result in the development of new life-saving drugs. The companies have had their way and, unless there are strong competitive restraints, have been able to set the prices for their medications at whatever level they choose or, as some would suggest, whatever the market will bear. A recent example is ipilimumab (Yervoy), an important new drug for the treatment of metastatic melanoma, for which the cost of a four-dose treatment regimen is approximately $120,000. And it is not just these intravenously-administered monoclonal antibodies for which the cost is high. For example, the cost of the important orally-administered antibiotic linezolid (Zyvox) is more than $100 for each tablet.

Although the high cost of medications is a continuing concern, it is mentioned here primarily for context in considering what I would suggest is a related issue – drug shortages – including situations in which certain life-saving medications are not available on a timely basis at any cost.

Shortages of drugs used to be isolated experiences. However, in 2011 alone, more than 200 drugs have been in short supply and some of these situations have reached crisis proportions. There have been serious shortages of medications used in surgery (e.g., propofol), critical care situations (e.g., furosemide, norepinephrine, labetalol), and the treatment of certain cancers (e.g., cytarabine). Patients with a diagnosis of cancer have a huge challenge in coping with the implications of their illness. They should not have to experience the additional uncertainties and anxiety as to whether the medications they need will be available, or the fear prompted by a call from the oncologist to cancel an appointment because the dose of the medication to be administered is not available. The American Society of Health-System Pharmacists is providing important leadership in increasing the awareness and urging action with respect to the shortages and the extremely important risks presented, and the Food and Drug Administration is doing much more to identify situations in which drug shortages exist or can be anticipated. However, progress has been slow and the need for action is urgent.

Contents



Consequences of Drug Shortages

Some of the medications for which there are shortages are life-saving drugs and patients may be endangered when they are not available on a timely basis. This is clearly the consequence that requires the highest priority attention.

Price-gouging has been another consequence of the shortages, with the prices requested for some drugs being 50 times their usual costs. An article titled, "Drug Shortages Lead to Price Gouging," (Liz Szabo in *USA Today*, August 18, 2011, p. 3D) begins:

> "Scalping tickets to a rock concert can get you arrested. But reselling lifesaving medications at a hefty markup is a thriving business."

The antihypertensive drug labetalol is often used in emergency situations and is one of the examples cited. The usual cost is approximately $25 a dose but some hospitals have been asked to pay as much as $1,200.

Shortage situations result in the development of a "gray market" in which drugs may not be available from the manufacturer or usual wholesaler(s), but can be obtained from "nontraditional" suppliers about whom little may be known. Such situations raise questions as to whether the stability and quality of the products have been maintained, and even whether counterfeit supplies of medication have been distributed in these secondary distribution channels. The profession of pharmacy should establish a "registry" of organizations and individuals who are involved as secondary suppliers of medications and/or in the sale of medications at prices that differ significantly from the usual price. This registry could have a Better Business Bureau-like role. Experiences of pharmacists who have purchased medications from these suppliers could be entered in the registry that could be accessed by other pharmacists considering such purchases.

There have been allegations that some of the current shortages may have been anticipated and that "speculators" were able to buy large quantities of these drugs that they were later able to sell at a much higher price. It does not require a leap of imagination to recognize that, for certain drugs, unscrupulous individuals could create a shortage by buying most of the supply at a relatively low price and reselling it at a much higher price when its availability has been artificially limited.

There are even allegations that some pharmaceutical companies may be using concerns about drug shortages as a scare tactic in the marketing strategies for certain of their drugs. This could be done by suggesting to pharmacies that they buy a larger-than-usual amount of a drug so that they would be assured of having an adequate supply in the event of a shortage. A variation of this strategy is to note that there is only a limited supply of an important drug (e.g., an anticancer drug) and, that to guarantee the continued availability of this medication for their patients, physicians should register them in a special program with the company.

Pharmaceutical Companies Must be Accountable

Most of the medications that are currently in short supply are not drugs for which sophisticated technology is required for their production or for which demand has unexpectedly and sharply increased. Various explanations for the shortages have been proposed including increased regulatory requirements and monitoring, less reliable sources of raw materials, and consolidation within the pharmaceutical industry. Some are advocating greater regulatory authority for the FDA and/or legislative action that would help prevent drug shortages. However, there has been too little attention given to the need for the pharmaceutical industry to be more accountable.

Many of the drugs for which shortages are of the greatest concern (i.e., life-saving or life-extending medications) are older drugs for which patents have expired resulting in their availability in less expensive generic formulations. These drugs are no longer highly profitable for the companies that developed and initially marketed them, and there is not an incentive for these companies to be certain that there are adequate supplies of these drugs available. Indeed, in a number of situations, a company that initially developed and marketed a drug that generated billions of dollars in profits during the period in which it had patent protection, discontinues marketing the drug or sells it to another company when generic equivalent products become available.

(Continued on Page 4)

New Drug Review

Lurasidone hydrochloride (Latuda – Sunovion)

Antipsychotic agent

New Drug Comparison Rating (NDCR) = 3

(no or minor advantages/ disadvantages) in a scale of 1 to 5, with 5 being the highest rating

Indication:
Treatment of patients with schizophrenia.

Comparable drugs:
Other atypical antipsychotic drugs (risperidone [e.g., Risperdal] is the specific agent to which comparisons are made).

Advantages:
- May be less likely to cause diabetes, weight gain, extrapyramidal symptoms, and hyperprolactinemia;
- Not likely to cause prolongation of the QT interval.

Disadvantages:
- Has not been directly compared with other antipsychotic agents in clinical studies;
- Labeled indications are more limited (risperidone is also indicated for the treatment of bipolar disorder and for the treatment of irritability associated with autistic disorder);
- May be more likely to cause somnolence/ sedation;
- Effectiveness and safety have not been established in pediatric patients;
- Fewer formulation options (risperidone is also available in an oral solution, orally disintegrating tablets, and an extended-release parenteral formulation).

Most important risks/adverse events:
Increased mortality in elderly patients with dementia-related psychosis (boxed warning; is not approved for the treatment of dementia-related psychosis); cerebrovascular adverse events; neuroleptic malignant syndrome; tardive dyskinesia; hyperglycemia and diabetes mellitus; dyslipidemia; hyperprolactinemia; leukopenia, neutropenia, and agranulocytosis; orthostatic hypotension and syncope; seizures; potential for cognitive and motor impairment (patients should be cautioned about engaging in activities requiring mental alertness); disruption of body temperature regulation; dysphagia; suicide (risk is inherent in psychiatric illness); is metabolized primarily via the CYP3A4 pathway and concurrent use with a strong CYP3A4 inhibitor (e.g., ketoconazole) or a strong CYP3A4 inducer (e.g., rifampin) is contraindicated.

Most common adverse events:
Somnolence (22%), akathisia (15%), nausea (12%), parkinsonism (11%), agitation (6%), anxiety (6%), dystonia (5%).

Usual dosage:
Recommended initial dosage – 40 mg once a day with food (at least 350 calories); maximum recommended dosage – 80 mg once a day with food; dosage should not exceed 40 mg/day in patients with moderate or severe renal impairment, moderate or severe hepatic impairment, or in

The pharmaceutical industry takes pride and credit, and rightfully so, for the development of life-saving drugs and many other medications that cure or effectively control numerous medical problems and/or greatly improve the quality of life. These companies justify the high prices for the medications they bring to the market by claiming that this revenue is needed to support the research programs that will result in the development of more life-saving drugs. However, if this pricing strategy of the companies is to be credible, and if the companies are to be recognized for the development of drugs that are of great value for patients, the companies must also accept the responsibility for assuring the availability of these drugs on a timely basis, even after patents have expired and they are available generically.

The pharmaceutical industry, collectively and as individual companies, must resolve the drug shortage problems that currently exist and should develop a system/strategy through which needed medications are available on an uninterrupted basis and shortages are avoided. One approach could be to have the FDA's initial approval of a drug include a commitment from the company to make supplies available on a timely basis unless, at some future time, there is agreement between the company and the FDA that there is no longer a valid need for the drug, or that arrangements deemed acceptable to the FDA are made through which the responsibility for supplying the drug is transferred to another company. In this latter situation, if a company is purchased by another company, the responsibility for maintaining the supplies of the medications would also be assumed by the purchasing company.

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New Drug Review (cont.)

patients treated concurrently with a moderate CYP3A4 inhibitor (e.g., diltiazem).

Products:

Tablets – 40 mg, 80 mg.

Comments:

Lurasidone is an atypical antipsychotic agent that is classified as a benzoisothiazol derivative. Its properties are most similar to those of risperidone, paliperidone (Invega), iloperidone (Fanapt), and ziprasidone (Geodon). Other atypical antipsychotic agents include aripiprazole (Abilify), asenapine (Saphris), clozapine (e.g., Clozaril), olanzapine (Zyprexa), and quetiapine (Seroquel). The effectiveness of lurasidone in the treatment of schizophrenia is thought to be mediated through a combination of central dopamine type 2 (D2) and serotonin type 2 (5HT2A) receptor antagonism. Its efficacy was demonstrated in four short-term (6-week) placebo-controlled studies in adult patients with schizophrenia. In three of the four studies each of the dosage regimens of lurasidone that was evaluated was superior to placebo, whereas in one study in which dosages of 40, 80, or 120 mg/day were used, only the 80 mg/day dosage was superior to placebo. In one study, one group of patients received olanzapine as an active control. Olanzapine was also demonstrated to be superior to placebo but the study was not powered to compare lurasidone with olanzapine. The peak serum concentration and bioavailability of lurasidone are increased when it is administered with food, and patients in the clinical studies were instructed to take the medication with food.

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